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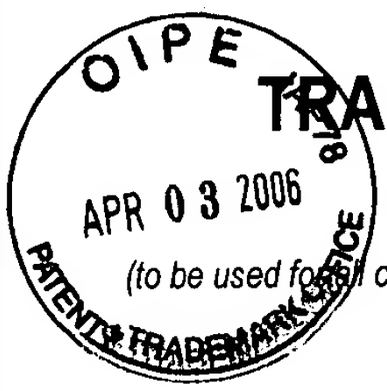

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First Named Inventor	Kevin P. Baker
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Examiner Name	Turner, Sharon L.
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ENCLOSURES *(check all that apply)*

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  - ☐ Fee Attached
- ☒ **Reply Brief**
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Turner, Sharon L.
Kevin P. BAKER, et al.	)	Art Unit: 1649
Application Serial No. 09/978,299	)	Confirmation No: 4234
Filed: October 15, 2001	)	Attorney's Docket No. 39780-2630 P1C3
For: **PRO195 POLYPEPTIDES**	)	**Customer No. 35489**

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ON APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPELLANTS' REPLY BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

On April 12, 2005, the Examiner made a Final Rejection to pending Claims 58-65 and 68-70. A Notice of Appeal was filed on September 12, 2005, and Appellants' Appeal Brief was filed November 10, 2005.

An Examiner's Answer was mailed on February 3, 2006. The following constitutes Appellants' Reply Brief in response to the Examiner's Answer. This Reply Brief is accompanied by a Request for Oral Hearing.

ARGUMENTS

Claim Rejections Under 35 U.S.C. §101

Claims 58-65 and 68-70 stand rejected under 35 U.S.C. §101 as allegedly lacking either a credible, specific and substantial asserted utility or a well established utility.

The Examiner asserts that the results of the adipocyte glucose/FFA uptake assay, showing that PRO195 tested positive as an inhibitor of glucose/FFA uptake in adipocyte cells, do not provide utility for the PRO195 polypeptides. In support of this assertion, the Examiner makes the following arguments:

(1) PRO195 is an inhibitor of glucose uptake and thus would not have utility in the treatment of disorders such as obesity, diabetes, and hyper- or hypo-insulinemia because it is desirable to stimulate glucose uptake in these conditions;

(2) inhibitors of PRO195 would not have utility because the instant specification does not teach that the PRO195 polypeptide is correlated with any specific disorders;

(3) the specification does not teach that PRO195 is involved in leptin regulation or that PRO195 could be used as a pharmacological tool for investigation of leptin regulation; and

(4) the proposed use of the claimed PRO195 polypeptides as a potential pharmacological tool to investigate leptin regulation is simply a starting point for further research and investigation into potential practical uses of the polypeptides.

The Examiner's arguments will be addressed in the order they are listed above.

The Examiner asserts that "the skilled artisan would not expect PRO195, which inhibits glucose uptake as asserted by the specification, to be beneficial to such disorders as obesity, diabetes, and hyper- or hypo-insulinemia, because in these conditions little or no glucose is entering the cells to begin with," and that therefore "one would expect the PRO195 polypeptide to *exacerbate* the condition." (Page 13 of the Examiner's Answer; see also pages 17-18, 21).

Appellants respectfully point out that the fact that PRO195 inhibits glucose uptake does not make it useless in such treatment. One of skill in the art would readily understand that a protein which inhibits glucose uptake into adipocytes is a useful therapeutic target, since blocking the function of this protein would decrease the inhibition, and thus increase glucose uptake into adipocytes. Accordingly, the claimed PRO195 polypeptides are useful in the therapeutic treatment of disorders wherein stimulation of glucose uptake by adipocytes is

expected to be therapeutically effective, such as obesity, diabetes, and hyper- or hypo-insulinemia.

With respect to inhibitors of PRO195, the Examiner asserts that "[t]here is simply no evidence or description of such a useful antagonist molecule and the suggestion is nothing more than a wish to know assertion." (Page 14 of the Examiner's Answer). Appellants respectfully submit that the specification has described antagonists of PRO195 function, for example, the antibodies specific for PRO195. See the specification at, for example, page 131, lines 1-2, and page 198, lines 3-6. Methods of making antibodies to PRO195 are disclosed at, for example, Example 104 and pages 217-220 of the specification, and methods of testing such antibodies for antagonist activity are disclosed at, for example, pages 196-199 of the specification. No further research or investigation is required to show that PRO195 is an inhibitor of glucose uptake, and that its function can be inhibited by molecules such as inhibitory antibodies. Accordingly, one of ordinary skill in the art would understand that inhibitors of PRO195, such as the disclosed antibodies, could be used in the treatment of disorders for which increased glucose uptake by adipocytes would be beneficial, such as diabetes, obesity, and hyper- and hypo-insulinemia, and would understand exactly how to make and use these antibodies, without any undue experimentation.

The Examiner asserts that inhibitors of PRO195 would lack utility because "the instant specification does not teach that the PRO195 polypeptide is even correlated with a disorder, particularly obesity, diabetes, and hyper- or hypo-insulinemia." The Examiner further notes that "the specification does not teach PRO195 protein expression levels in normal or diseased subjects" and concludes that "[i]n order for a polypeptide to be useful, as asserted, for diagnosis or treatment of a disease, there must be a well-established or disclosed correlation or relationship between the polypeptide and a disease or disorder." (Page 13 of the Examiner's Answer; see also pages 18, 21-22).

Appellants respectfully submit that the facts of the instant situation are similar to those in as *Nelson v. Bowler,*[1] in which the claims at issue were directed to 16-phenoxy prostaglandins which showed activity in stimulation of smooth muscle tissue from gerbil colons and modulation of blood

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[1] *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

pressure in rats. Although Nelson admitted that antifertility activity such as luteolysis was not proven by these tests, the Court concluded nonetheless that "tests evidencing pharmacological activity may manifest a practical utility **even though they may not establish a specific therapeutic use**"[2] (emphasis added). The court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."[3] Accordingly, it is not necessary to demonstrate that PRO195 or its inhibitors have a specific therapeutic use in the treatment of a particular disease. The disclosure that PRO195 has a pharmacological activity, regulation of glucose and FFA transport in adipocytes, is sufficient to demonstrate utility for PRO195.

Appellants also point out that Mueller *et al.* (1998) disclose that inhibitors of adipocyte glucose uptake, including 2-DG, phloretin, and cytocholasin B, inhibit leptin gene expression and leptin secretion from adipocytes. It was known in the art at the time of filing that leptin is involved in the regulation of food intake, energy expenditure, and body fat stores, and that leptin decreases after fasting or caloric restriction and increases a number of hours after refeeding. (Mueller *et al.* (1998), p. 551, col. 1). One of skill in the art would therefore have understood that agents capable of modulating leptin regulation would be useful in investigations regarding the treatment of obesity. Similarly, PRO195, as an inhibitor of adipocyte glucose uptake, would be useful as a pharmacological tool for investigation of leptin regulation and obesity, in the same way as agents already known and used in the art such as 2-DG, phloretin, and cytocholasin B.

The Examiner asserts that the specification "does not teach that PRO195 is involved in leptin regulation or that PRO195 could be used as a pharmacological tool for investigation of leptin regulation." (Page 14 of the Examiner's Answer; see also page 19).

As discussed above, Mueller *et al.* (1998) demonstrated that insulin-induced increases in leptin secretion were more closely related to the amount of glucose taken up by the adipocytes than to the insulin concentration, suggesting a role for glucose transport and/or metabolism in regulating leptin secretion. Mueller *et al.* further demonstrated that both metformin and

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[2] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

[3] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

vanadium increased glucose uptake and inhibited leptin secretion from cultured adipocytes. (Muller *et al.*; 2000). Thus it was known in the art at the time of filing that molecules which regulated glucose uptake by adipocytes also, as a consequence, regulated leptin secretion. The specification clearly discloses that PRO195 is an inhibitor of glucose uptake into adipocyte cells; thus one of ordinary skill in the art would understand that as a necessary consequence of regulating adipocyte glucose uptake, PRO195 would also affect leptin secretion. Thus PRO195 would be useful as a pharmacological tool for investigation of leptin regulation and the disorders with which it is associated, such as obesity.

The Examiner asserts that "the proposed use of the claimed PRO195 polypeptides as a potential therapeutic tool to investigate leptin regulation is simply a starting point for further research and investigation into potential practical uses of the polypeptides." (Page 14 of the Examiner's Answer; see also page 19). In support of this assertion, the Examiner cites Mueller 2000 to the effect that "[f]urther research, including examination of the potential roles of glucose oxidation and lipogenesis, needs to be conducted to determine the precise biochemical and molecular mechanisms by which glucose metabolism regulates leptin production." (Page 19 of the Examiner's Answer). Appellants respectfully point out that the "further research" described in Mueller 2000 is not directed towards finding practical utilities for glucose uptake inhibitors such as 2-DG, phloretin, cytocholasin B, or PRO195. Rather, the further research is directed towards understanding the mechanisms through which glucose regulates leptin production. In order to conduct such research, it is necessary to have a means of reliably controlling the key variable of how much glucose enters the leptin-secreting adipocyte cells. Glucose uptake inhibitors such as PRO195 have practical utility in enabling researchers to conduct such experiments, by providing a method of controlling the amount of glucose taken up by the adipocytes.

The Examiner asserts that "[w]hereas a scale or a microarray or a gas chromatograph has patentable utility as a research tool, the objects being evaluated with these research tools do not necessarily have patentable utility." (Page 15 of the Examiner's Answer; see also page 24). Appellants respectfully point out that the proposed use of PRO195 is not as an object of research. The research in which PRO195 is involved is the study of glucose metabolism and leptin regulation. PRO195 is useful in such research because it provides researchers with a tool that enables them to control the amount of glucose taken up by leptin-secreting adipocyte cells.

Appellants have previously pointed out in their Appeal Brief that the Patent Office routinely issues patents for inventions whose only use is to facilitate research, such as the DNA ligases of Example 10 of the Revised Interim Utility Guidelines Training Materials. The Examiner asserts that "DNA ligases have a well-established utility in the art based on this class of proteins' ability to ligate DNA. Also, the literature discloses many DNA ligases which have been fully characterized at the structural and functional level." (Page 25 of the instant Office Action). Appellants respectfully submit that the family of glucose uptake inhibitors, including, for example, 2-DG, phloretin and cytocholasin B, also have a well-established utility in the art, as discussed above. As evidenced by this list of glucose uptake inhibitors, it is clear that the literature discloses many members of the family which have been structurally and functionally characterized. Thus the family of glucose uptake inhibitors meets the same standards as the family of DNA ligases.

As the Patent Office acknowledges, there are many research situations in which researchers need tools for ligating a DNA; hence DNA ligases have utility. It is equally true that there are research situations in which researchers need tools for controlling the amount of glucose uptake by adipocyte cells; hence molecules which inhibit glucose uptake are useful. The Patent Office continues to incorrectly assert that Appellants have proposed using PRO195 as an object of research, while not addressing Appellants' evidence that PRO195 has a specific activity as a glucose uptake inhibitor, and that molecules with this activity have known uses as research tools.

Finally, the Examiner asserts that "the claimed PRO195 polypeptide is not disclosed in any association with disorders associated with altered glucose uptake where such experimentation is the result of a significance, association or as having an activity that can be specifically useful" and concludes that "if the specification discloses nothing specific and substantial about the PRO195 polypeptide, therefore both the polypeptide and its inhibitory molecules (e.g., antibodies) have no patentable utility." (Pages 24-25 of the Examiner's Answer).

Appellants note that the specificity requirement is not an onerous one. The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information

about the utility of what is being claimed.[4] Such is clearly not the case here. The asserted utility for the claimed polypeptides is not based upon vague "biological properties," but a specific activity, inhibition of glucose uptake by adipocytes. This activity has already been demonstrated, as shown in Example 117 of the specification. As demonstrated by publications such as Mueller (2000) and references 28-30 cited therein, molecules which inhibit glucose uptake by adipocytes have a well-established use as research tools. Accordingly, PRO195 has a specific utility in the study of disorders associated with altered glucose uptake by adipocytes, such as diabetes, obesity, and hyper- and hypo-insulinemia.

Appellants further note that the subset of research uses that are not "substantial" utilities is limited. It consists only of those uses in which the claimed invention is to be an **object** of further study, thus merely inviting further research on the invention itself. This follows from *Brenner v. Mason*, in which the U.S. Supreme Court held that a process for making a compound does not confer a substantial benefit where the only known use of the compound was to be the object of further research to determine its use.[5]

As discussed above, beneficial uses beyond studying the claimed invention itself have been demonstrated for PRO195, in particular, the study of disorders associated with altered glucose uptake by adipocytes, such as diabetes, obesity, and hyper- and hypo-insulinemia. Accordingly, the claimed PRO195 polypeptides have a specific and substantial utility.

The case law has clearly established that Appellants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face.[6] The Examiner has the initial burden that Appellants' claims of usefulness are not believable on their face.[7] In general, an Appellant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."[8], [9] Indeed, the Guidelines for

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[4] *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

[5] *Brenner v. Manson,* 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

[6] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[7] *Ibid.*

[8] *In re Langer*, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (C.C.P.A. 1974).

Examination of Applications for Compliance With the Utility Requirement,[10] gives the following instruction to patent examiners: "If the Applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

As discussed above and in Appellants' Brief, the instant specification and the known art at the time of filing clearly demonstrate that PRO195 has an activity, inhibition of glucose uptake by adipocytes, that is useful for practical purposes. In particular, PRO195 has at least two different types of practical utilities. PRO195 is useful as a target in screening assays to identify agents that increase glucose uptake, and could be used therapeutically in the treatment of diseases such as disorders such as obesity, diabetes, and hyper- or hypo-insulinemia. PRO195 is also useful in the investigation of glucose uptake and the mechanisms of diseases related to glucose uptake, such as obesity, diabetes, and hyper- or hypo-insulinemia.

Accordingly, for at least the above reasons, the results of the adipocyte glucose/FFA uptake assay provide a specific, substantial and credible utility for the claimed PRO195 polypeptides.

Claim Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

Claims 58-65 and 68-70 stand rejected under 35 U.S.C. §112, first paragraph, for essentially the same reasons as discussed above. Appellants respectfully submit that as described above, the PRO195 polypeptides have utility in the treatment of disorders for which modulation of glucose uptake by adipocytes would be beneficial, such as obesity, diabetes, and hyper- or hypo-insulinemia, or as pharmacological tools for the study of these diseases and conditions, and based on such a utility, one of skill in the art would know exactly how to use the claimed polypeptides without undue experimentation.

The Examiner's Answer further maintains that even if the polypeptide of SEQ ID NO:330 were to have a patentable utility, the specification does not provide enablement for the claimed

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[9] *See also In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 U.S.P.Q. 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 U.S.P.Q. 209, 212-13 (C.C.P.A. 1977).

[10] M.P.E.P. §2107 II (B)(1).

variant polypeptides having at least 80% identity to SEQ ID NO:330 wherein the polypeptide inhibits the uptake of glucose or FFA (free fatty acid) by adipocyte cells.

The Examiner asserts that "[t]he specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such trial and error experimentation is considered undue." (Page 30 of the Examiner's Answer). Appellants respectfully point out that the disclosure provided in the specification does not constitute mere trial and error experimentation, because the specification detailed guidance as to the types of changes that may be made to a PRO polypeptide without adversely affecting its activity (page 180, line 9 to page 183, line 8). This guidance includes a listing of exemplary and preferred substitutions for each of the twenty naturally occurring amino acids (Table 6, page 182).

The Examiner further asserts that "the skilled artisan would not be able to determine, without undue experimentation, the structural conformation and function of PRO195 variants based upon linear amino acid sequences only." (Page 31 of the Examiner's Answer). In support of this assertion, the Examiner cites Skolnick *et al.* and Jobling *et al.* to the effect that "function cannot be predicted from structure." (Page 30 of the Examiner's Answer). Appellants note that, as discussed in their Appeal Brief, Skolnick *et al.* says nothing about the effects of single amino acid substitutions on the function of known proteins, while Jobling *et al.* confirms that most single amino acid changes, particularly conservative changes, do not affect protein structure or function.

Appellants further note that functional activity in this instance is not claimed based solely on structural similarity, but instead based on the positive results in the adipocyte glucose/FFA uptake assay. As discussed above, Appellants claim only those proteins which meet both recitations of the claims, structural and functional. The claims are not directed to all possible variants having at least 80% amino acid sequence identity to SEQ ID NO:330, but only to those variants which retain the function of the polypeptide as an inhibitor of glucose/FFA uptake by adipocytes. The specification provides the protocol for the adipocyte glucose/FFA uptake assay, as disclosed in Example 117. It would be a simple matter for one skilled in the art to test the variant polypeptides generated according to the guidance provided in the specification, to see if they are inhibitors of glucose/FFA uptake by adipocytes using the methods of Example 117. This would not require undue experimentation.

The Examiner asserts that "the broad brush discussion of making and screening for variants does not constitute a disclosure of a representative number of members." (Page 32 of the Examiner's Answer). Appellants respectfully submit that the claimed genus includes only those variants having both the recited activity of inhibiting the uptake of glucose or FFA by adipocyte cells and having at least 80% identity to SEQ ID NO:330. When both the structural and functional limitations are included, the genus is limited to a size where the demonstrated species suffices to represent the genus.

The claims currently recite peptide sequences associated with a biological activity. This biological activity together with the well defined relatively high degree of sequence identity and general knowledge in the art at the time the invention was made, sufficiently defines the claimed genus such that, one skilled in the art, at the effective date of the present application, would have known how to make and use the claimed peptide sequences without undue experimentation. As the M.P.E.P. states, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."[11]

As discussed above, a considerable amount of experimentation is permissible, if it is merely routine. Appellants submit that the identification of variant PRO195 polypeptides having at least 80% identity to SEQ ID NO:330 wherein the polypeptide inhibits the uptake of glucose or FFA by adipocyte cells can be performed by techniques that were well known in the art at the priority date of this application, and that the performance of such work does not require undue experimentation.

Accordingly, Appellants respectfully request reconsideration and reversal of the enablement rejection of Claims 58-65 and 68-70 under 35 U.S.C. §112, first paragraph.

Claim Rejections Under 35 U.S.C. §112, First Paragraph - Written Description

Claims 28-35 and 38-40 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to provide adequate written description for the claimed variant polypeptides having at least 80% amino acid sequence identity to SEQ ID NO:330, wherein the polypeptide inhibits the uptake of glucose or FFA (free fatty acid) by adipocyte cells.

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[11] M.P.E.P. §2164.01 citing *In re Certain Limited-charge Cell Culture Microcarriers,* 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff' sub nom. Massachusetts Institute of Technology v. A.B. Fortia*, 774 F 2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

Appellants respectfully reiterate that Claim 63 (and, as a consequence, claims 64-65 and 68 dependent from the same), do not recite variant polypeptides, but are directed to the polypeptide of SEQ ID NO:330, with or without its signal peptide sequence. The Examiner has acknowledged that Appellants have described the polypeptide sequence of SEQ ID NO:330. (Page 7 of the Office Action mailed April 12, 2005). As disclosed, for example, in Figure 132, the signal peptide sequence of SEQ ID NO:330 comprises amino acid residues 1-31. Accordingly, the specification has clearly described the polypeptide of SEQ ID NO:330, with or without its signal peptide, and thus the subject matter of Claims 63-65 and 68 meets the written description requirement under 35 U.S.C. §112, first paragraph.

With respect to the claimed variant polypeptides of Claims 58-62 and 69-70, the Examiner asserts that "the only factors present in the claims are a partial structure in the form of a recitation of percent identity and a requirement that the polypeptide inhibits the uptake of glucose or FFA in adipocyte cells. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function." (Page 36 of the Examiner's Answer).

Applicants respectfully submit that the U.S.P.T.O. Written Description Guidelines do not require a structure-function relationship. Page 8 of the Written Description Guidelines notes five factors provided for analysis for compliance with the written description guidelines: a) partial structure; b) physical and/or chemical properties; c) functional characteristics; d) known or disclosed correlation between structure and function; e) method of making; and f) combinations of any of these factors. A structure-function correlation is only one possible factor. A combination of other factors, such as partial structure, functional characteristics, and method of making, all of which are disclosed for the instantly claimed variants, is also sufficient to provide written description.

Furthermore, Example 14 of the Synopsis of Application of Written Description Guidelines issued by the U.S. Patent Office clearly states that protein variants meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins are routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the

variant proteins possess the specified functional activity and a defined degree of sequence identity to the reference sequence. The instant claims are in the format exemplified by Example 14. As discussed in Appellants' Brief, the procedures for making the claimed variant proteins are well known in the art and described in the specification. The specification also provides an assay, shown in Example 117, for detecting the recited functional activity of the claimed variants. Finally, the claimed variant proteins possess both the specified functional activity and a defined degree of sequence identity to the reference sequence, SEQ ID NO:330. Accordingly, the claimed variants meet the standards set forth in the Written Description Guidelines and exemplified by Example 14.

The Examiner asserts that "the fact pattern in the instant application is not analogous to Example 14 in the Revised Interim Written Description Guidelines." In particular, the Examiner asserts that the protein of Example 14 is an enzyme, and that "such an enzyme would have a conserved structure that is responsible for the enzyme activity. Thus it is likely predictable, based upon percent identity, which variant would share the same function." (Page 37 of the Examiner's Answer).

The PTO's attempts to distinguish the instant claims from those of Example 14 are based upon reading into Example 14 additional details that are unsupported by the actual text of the Guidelines. There is no indication in Example 14 that the specification provided any description of particular sequences required for enzymatic activity. Example 14 states only that the specification "indicates that procedures for making proteins with substitutions, deletions, insertions and additions are routine in the art and provides an assay for detecting the catalytic activity of the protein." This is equivalent to the disclosure provided in the instant specification.

The Examiner asserts that "[t]he broad brush discussion of making and screening for variants in the instant specification does not constitute a disclosure of a representative number of species." (Pages 35, 37 of the Examiner's Answer). This assertion is incorrect because the claimed genus includes only those variants having both the recited activity of inhibiting the uptake of glucose or FFA by adipocyte cells and having at least 80% identity to SEQ ID NO:330. When both the structural and functional limitations are included, the genus is limited to a size where the demonstrated species suffices to represent the genus.

As discussed above, the claimed sequences are defined both by a structural limitation (having at least 80% amino acid sequence identity to a described reference sequence), and by a functional limitation, (having a specific biological activity, as measured by specific, disclosed assays). The specification also discloses methods of making the recited polypeptide variants. The instant claims and specification thus include all of the factors accepted in Example 14 of the Written Description Guidelines as sufficient to provide written description for a claimed genus of polypeptides. Accordingly, the recited biological activity, coupled with a well defined, and relatively high degree of sequence identity, sufficiently defines the claimed genus such that one skilled in the art would readily recognize that the Appellants were in the possession of the invention claimed at the effective filing date of this application.

CONCLUSION

For the reasons given above, Appellants submit that the adipocyte glucose/FFA uptake assay disclosed in Example 117 of the specification provides at least one asserted specific and substantial patentable utility for the claimed PRO195 polypeptides, and that one of ordinary skill in the art would accept this asserted utility as credible and would understand how to make and use the claimed polypeptides. Therefore, claims 58-65 and 68-70 meet the requirements of 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph.

Appellants further submit that Claims 58-65 and 68-70 meet the written description requirement of 35 U.S.C. §112, first paragraph.

Accordingly, reversal of all the rejections of Claims 58-65 and 68-70 is respectfully requested.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2630 P1C3**).

Respectfully submitted,

Date: April 3, 2006

By: _____
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